REMARKS

The Status of the Claims and the Amendments

Applicants respectfully thank the Examiner for withdrawing the finality of the previous Office Action and entering Applicants' after final amendment and response dated February 19, 2009.

In the present matter the Examiner has suggested that the previous amendment to base claims 1 and 13 have allegedly improperly broadened the claims beyond a previous species restriction. Without acquiescing to the reasoning of the Office, Applicants have amended the claims to replace "DNA molecule" with "oligodeoxynucleotide." These amendments were originally supported throughout the specification in general and more specifically in examples 12-15 and therefore do not constitute new matter.

§112, First Paragraph Rejections.

Claims 1-22 stand rejected under 35 USC §112, first paragraph for allegedly failing to comply with the written description requirement. The Examiner graciously suggests that an amendment of base claims 1 and 13 replacing "DNA molecule" with "oligodeoxynucleotide" would obviate the rejection. Therefore, without acquiescing to the reasoning of the Office, claims 1 and 13 have been amended to replace "DNA molecule" with "oligodeoxynucleotide".

Applicants respectfully request that the rejection be withdrawn.

Claims 1-22 additionally stand rejected under 35 USC §112, first paragraph for allegedly failing to comply with the enablement requirement. The Examiner has modified the rejection to indicate an enabled scope for the invention, wherein the specification is enabled for a composition for the elicitation of a systemic non-antigen specific immune response in a mammal comprising :a. a liposome delivery vehicle; and b. an oligodeoxynucleotide containing no CPG

motifs and from more than 25 to about 100 nucleotides in length; wherein said composition elicits a systemic, non antigen specific Th1 immune response in said mammal; and a method comprising administering to a mammal an amount of said composition effective to elicit a Th1 immune response. The Examiner alleges that the present claim amendments are not sufficiently enabled for said method or composition as a therapeutic, or wherein the non-CpG motifs are present in any DNA molecule, as broadly claimed.

Applicants respectfully traverse the rejection. Without acquiescing to the reasoning offered by the Office, and in order to expedite prosecution of the instant application claims 1 and 13 have been amended as stated above to replace "DNA molecule" with "oligodeoxynucleotide". Additionally, claim 1 has been amended to remove the word "therapeutic" before composition. These amendments are made without prejudice and Applicant reserves the right to file continuation or divisional applications containing the above subject matter. In light of the listed amendments this rejection should be rendered moot. Therefore, reconsideration and withdrawal of this rejection is respectfully requested.

Applicants respectfully request that the rejection be withdrawn.

§103, Obviousness Rejections

Claims 1-7, 10, 13-19 and 22 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Auf et al (Clin. Cancer Res. 2001), in view of Vollmer et al. (Antisense & Nucl. Acid Drug Dev. 2002) and further in view of Tam et al., (U.S. Patent Publication No.:2004/0009944). Applicants respectfully traverse the rejection as applied to the pending claims.

The Examiner summarizes that Auf et al. describe phosphothorioate oligodeoxynucleotides containing CpG motifs that display immunostimulating activity without antigen, in rats and mice, inducing tumor rejections through an early activation of innate

immunity and priming or a specific immune response against glioma cells. Additionally the Examiner asserts that Auf et al describe a 22mer oligodeoxynucleotide in which the CpG motifs have been mutated resulted in a lesser reduction in tumor volume than a corresponding oligodeoxynucleotide containing two CpG motifs. (Figure 1).

Applicants respectfully disagree that Auf et al does anything but teach away from a composition comprising a liposome delivery vehicle and an oligodeoxynucleotide from more than about 25 to about 100 nucleotides in length containing no CpG motifs, having the ability to elicit a systemic non-antigen specific Th1 immune response in a mammal. Regarding Figure 1, the authors state below the figure that the IMM-ODNs did not lead to significant tumor reduction, and in the discussion of all of the results for the manuscript Auf states that "CpG motifs within the ODN were critical to trigger the immune response, for an ODN without such motifs was inefficient."

Additionally, the Examiner has pointed out that the oligodeoxynucleotides described by Auf having no CpG motifs was not greater than 25 nucleotides in length, and was not administered with a liposome delivery vehicle.

The Examiner attempts to bolster the shortcomings of Auf with Vollmer et al. which according to the examiner describe highly immunostimulatory CpG-free oligodeoxynucleotides for activation of human leukocytes , and less efficient in stimulating human immune cells. According to the Examiner, Vollmer et al specifically describe CpG-free oligodeoxynucleotides having 27 and 30 nucleotides in length in Table 1, thus curing the deficiency in Auf for oligodeoxynucleotide length. Applicants respectfully traverse for the reasons stated above regarding Auf and the following reasons for Vollmer.

Although Vollmer comprises immunostimulatory CpG-free oligodeoxynucleotides it comprises the use of methylated CpG ODNs to stimulate a Th2 immune response and actually

teaches away from using non-methylated CpG ODNs to stimulate a Th1 as described and or claimed in the present invention. Column 2 on page 173 in the discussion of Vollmer states "the 20-mer thymidine homopolymer used for these studies gave a Th2-like antibody response on immunization, in contrast to Th1-like responses with CpG ODNs." And that "*in vitro* longer non-CpG thymidine rich ODNs are always less efficient and potent than CpG ODNs, and, therefore, they might induce weaker *in vivo* effects that are not sufficient to mediate efficiently a Th1-dominated immune response."

The Examiner further attempts to bolster the Auf and Vollmer references with Tam et al., because Tam describes immunostimulatory oligonucleotides bearing methylated CpG dinucleotide motifs encapsulated in a lipid particle. However, teaching the mere concept of the lipid particle does not overcome the shortcomings previously described for the Auf and Vollmer references in teaching the present invention.

The Examiner additionally argues that the composition and methods described by Auf Vollmer and Tam are directed to oligodeoxynucleotides to elicit an immune response. Thus a person of ordinary skill in the art would have been motivated to combine their respective teachings to elicit a systemic non-antigen specific immune response in a mammal. Applicants respectfully disagree, for the reasons stated above, which show that the references all teach different kinds of ODNs or entirely different targets, and/or mechanisms and results. When combined the references would not assist one to create the composition as presently claimed.

Applicants submit that the cited references neither teach or suggest a composition comprising a liposome delivery vehicle and an oligodeoxynucleotide from more than 25 to about 100 nucleotides in length containing no CpG motifs, having the ability to elicit a systemic non-antigen specific Th1 immune response in a mammal, and a method comprising administering said composition to a mammal decribed in the claims as presently amended. Thus, the cited references do not teach all of the elements of the present claims. Moreover, absent the teachings

of the present application, there is no motivation to modify the methods of the cited references to include the present invention. Because as stated above the references actually teach away from the results and claims of the present invention there would be no motivation to combine the references to reach teach all of the elements of the present claims.

Claims 1, 7-9, 13 and 19-21 were additionally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Auf et al (Clin. Cancer Res. 2001), in view of Vollmer et al. (Antisense & Nucl. Acid Drug Dev. 2002) and Tam et al., (U.S. Patent Publication No.:2004/0009944), and further in view of Klinman (U.S. Patent Publication No.:2003/0060440). Applicants respectfully traverse the rejection as applied to the pending claims for all of the reasons stated above.

In regards to Klinman et al., the examiner attempts to use the reference to bolster the above references based on the fact that Klinman describes the use of aqueous dextrose in the formulation. Like Auf, and Tam, Klinman is used when formulating CpG motifs for inducing an immune response. Klinman therefore, does not overcome the previously identified shortcomings of the Auf and Vollmer references.

Applicants submit for the reasons stated above that the cited references do not teach all of the elements of the present claims. Moreover, absent the teachings of the present application, there is no motivation to modify the methods of the cited references to include the present invention.

Based on the foregoing, Applicants submit that the claimed methods are not obvious in view of the cited references. Accordingly, reconsideration and withdrawal of rejection of the claims under 35 U.S.C. § 103 are respectfully requested

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims 1-10 and 13-22 are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

The Commissioner is hereby authorized to charge $490.00 as payment for the Petition for Two-Month Extension of Time. Additionally, the Commissioner is hereby authorized to charge any fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896, referencing the above-identified docket number.

Respectfully submitted,

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